

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2004D-0378]

ADM
SEP 10 2004
Display Date _____
Publication Date SEP 13 2004
Certifier *SKP*

**International Conference on Harmonisation; Draft Guidance on S7B
Nonclinical Evaluation of the Potential for Delayed Ventricular Repolarization
(QT Interval Prolongation) by Human Pharmaceuticals; Availability**

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a revised draft guidance entitled “S7B Nonclinical Evaluation of the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals.” The draft guidance was prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The draft guidance describes a nonclinical testing strategy for assessing the potential of a test substance to delay ventricular repolarization and includes information concerning nonclinical assays and an integrated risk assessment. The draft guidance is intended to facilitate the nonclinical assessment of the effects of pharmaceuticals on ventricular repolarization and proarrhythmic risk.

DATES: Submit written or electronic comments on the draft guidance by *[insert date 90 days after date of publication in the Federal Register]*.

ADDRESSES: Submit written comments on the draft guidance to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630

Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>. Submit written requests for single copies of the draft guidance to the Division of Drug Information (HFD–240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857; or the Office of Communication, Training and Manufacturers Assistance (HFM–40), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448. The guidance may also be obtained by mail by calling the CBER Voice Information System at 1–800–835–4709 or 301–827–1800. Send two self-addressed adhesive labels to assist the office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the revised draft guidance document.

FOR FURTHER INFORMATION CONTACT:

Regarding the guidance: John Koerner, Center for Drug Evaluation and Research (HFD–110), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–5338.

Regarding the ICH: Michelle Limoli, Office of International Programs (HFG–1), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–4480.

SUPPLEMENTARY INFORMATION:

I. Background

In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonization of regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking scientifically based harmonized technical procedures for pharmaceutical

development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory agencies.

ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission; the European Federation of Pharmaceutical Industries Associations; the Japanese Ministry of Health and Welfare; the Japanese Pharmaceutical Manufacturers Association; the Centers for Drug Evaluation and Research and Biologics Evaluation and Research, FDA; and the Pharmaceutical Research and Manufacturers of America. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization, Health Canada, and the European Free Trade Area.

In the **Federal Register** of June 14, 2002 (67 FR 40950), the agency made available a draft guidance entitled “S7B Safety Pharmacology Studies for Assessing the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals” and invited public comment. After considering the comments, the Safety Expert Working Group of the ICH made extensive changes to the document, including changes to the title of the draft

guidance, the testing strategy, and the timing of nonclinical studies relative to clinical development.

In June 2004, the ICH Steering Committee agreed that a revised draft guidance entitled “S7B Nonclinical Evaluation of the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals” should be made available for public comment. Comments about this draft will be considered by FDA and the Safety Expert Working Group.

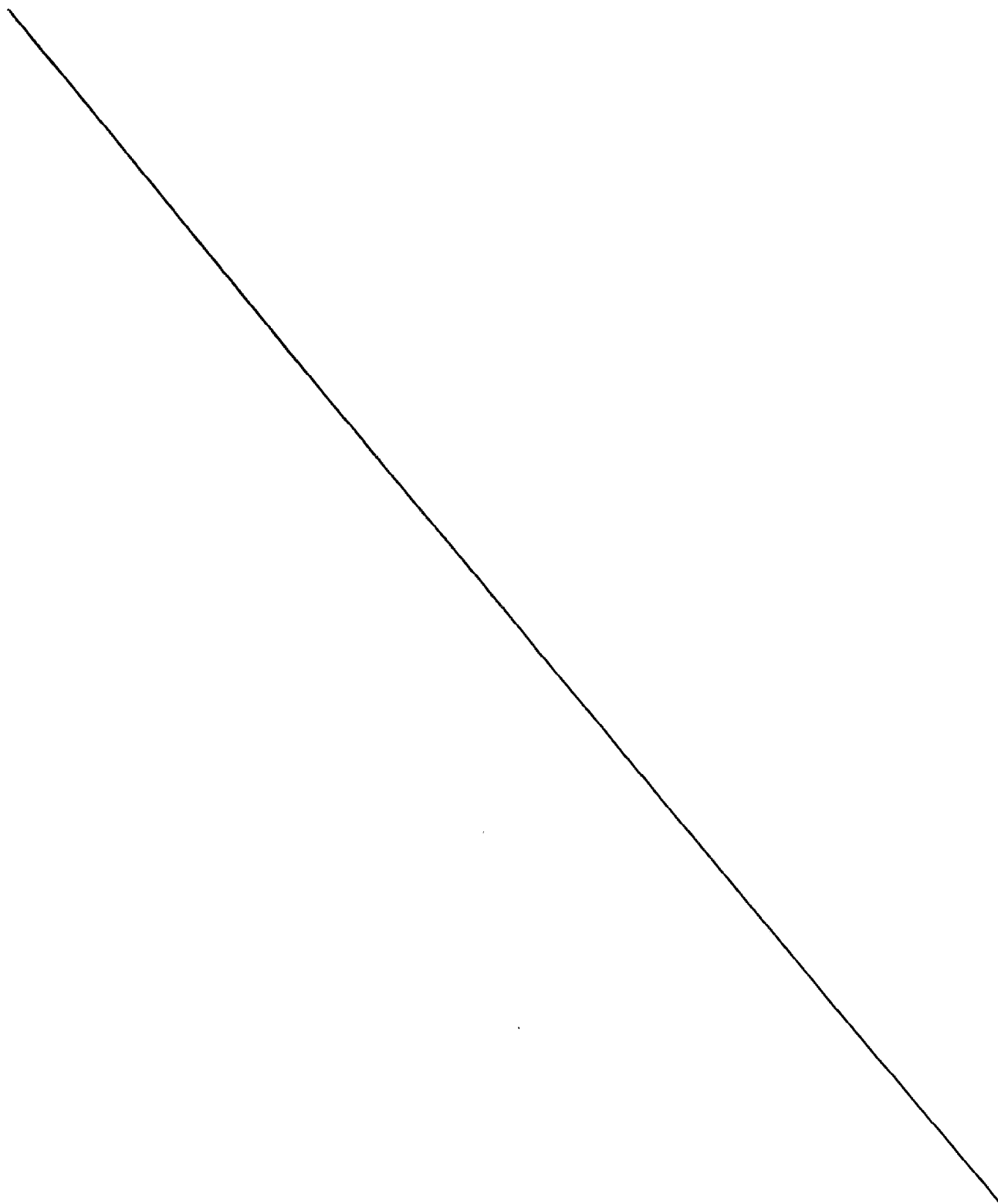
The draft guidance provides guidance on nonclinical assessment of the effects of pharmaceuticals on ventricular repolarization and proarrhythmic risk. The draft guidance describes a nonclinical testing strategy for assessing the potential of a test substance to delay ventricular repolarization and includes information concerning nonclinical assays and an integrated risk assessment.

This draft guidance, when finalized, will represent the agency’s current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments on the draft guidance. Submit a single copy of electronic comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft guidance and received comments may be seen in the

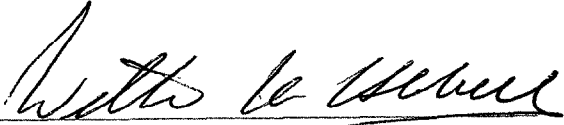
Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.



III. Electronic Access

Persons with access to the Internet may obtain the document at <http://www.fda.gov/ohrms/dockets/default.htm>, <http://www.fda.gov/cder/guidance/index.htm>, or <http://www.fda.gov/cber/publications.htm>.

Dated: September 3, 2004
September 3, 2004.



William K. Hubbard,
Associate Commissioner for Policy and Planning.

[FR Doc. 04-????? Filed ??-??-04; 8:45 am]

BILLING CODE 4160-01-S

